

characterized by a ligand binding specificity or by the presence of suitable epitopes which allows a selective purification preferably by affinity chromatography methods, e.g., by way of immobilized ligands or immobilized antibodies. Such affinity modules always have the property of binding ligands very specifically and with high binding constants, which in turn are preferably coupled as ligands to chromatographic matrices. In this way, highly purified fusion proteins from lysates or cell supernatants can be produced using processes with only few steps. --

In the Claims:

Please cancel claim 32 without prejudice.

Please amend claims 1, 15, 17, 18, and 33-37 to read as follows:

1. (Amended) A nucleic acid molecule encoding a fusion protein which comprises
(a) an effector module which is intracellularly cytotoxic, the effector module comprising one of a mistletoe lectin A chain, a fragment thereof, and a derivative thereof, wherein the mistletoe lectin A chain is encoded by a nucleic acid molecule selected from the group consisting of:

- (i) a nucleic acid molecule which has a nucleotide sequence encoding at least a fragment of a protein having the amino acid sequence SEQ ID NO: 2;
- (ii) a nucleic acid molecule having the nucleotide sequence of at least a fragment of SEQ ID NO: 1;
- (iii) a nucleic acid molecule which hybridizes with the nucleic acid molecule of (i) or (ii); and
- (iv) a nucleic acid molecule which is degenerate with respect to the nucleic acid molecule of (iii);

(b) a processing module which is covalently linked to the effector module and which comprises a recognition sequence for a protease, wherein the processing module comprises one of a mistletoe lectin propeptide, a fragment thereof, and a derivative thereof, and wherein the mistletoe lectin propeptide is encoded by a nucleic acid molecule selected from the group consisting of:

- (i) a nucleic acid molecule which has a nucleotide sequence encoding at least a fragment of a protein having the amino acid sequence SEQ ID NO: 6;

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- (ii) a nucleic acid molecule having the nucleotide sequence of at least a fragment of SEQ ID NO: 5;
 - (iii) a nucleic acid molecule which hybridizes with the nucleic acid molecule of (i) or (ii); and
 - (iv) a nucleic acid molecule which is degenerate with respect to the nucleic acid molecule of (iii); and
- (c) a targeting module which is covalently linked to the processing module and which specifically binds to the surface of a cell, thereby mediating internalization of the fusion protein into the cell.
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15. (Twice amended) The nucleic acid molecule of claim 7, wherein the affinity module comprises a portion selected from the group consisting of a histidine sequence, thioredoxin, maltose-binding protein, green fluorescent protein, SEQ ID NO.: 39, and an 11 amino acid T7 gene leader peptide.

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17. (Amended) The nucleic acid molecule of claim 16, wherein the mistletoe lectin B chain has at least one amino acid exchange at an amino acid position selected from the group consisting of positions 23, 38, 79, 235, and 249.

18. (Amended) The nucleic acid molecule of claim 17, wherein the exchange is selected from the group consisting of substitution of A at position D23, substitution of A at position W38, substitution of A at position D235, and substitution of A at position Y249.

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33. (Amended) A kit, comprising at least one of

- (a) a vector which comprises the nucleic acid molecule of claim 1; and
- (b) a vector which comprises the nucleic acid molecule of claim 7;

and a vector which comprises a nucleic acid molecule encoding a modulator which modulates the intracellular cytotoxicity of the effector module of (a) and/or (b).

34. (Amended) A nucleic acid molecule encoding a fusion protein which comprises

- (a) an effector module which is intracellularly cytotoxic, the effector module comprising one of a mistletoe lectin A chain, a fragment thereof, and a derivative thereof,

wherein the mistletoe lectin A chain is encoded by a nucleic acid molecule selected from the group consisting of:

- (i) a nucleic acid molecules which has a nucleotide sequence encoding at least a fragment of a protein having the amino acid sequence SEQ ID NO: 2;
 - (ii) a nucleic acid molecule which has the nucleotide sequence of at least a fragment of SEQ ID NO: 1;
 - (iii) a nucleic acid molecule which hybridizes with the nucleic acid molecule of (i) or (ii); and
 - (iv) a nucleic acid molecule which is degenerate with respect to the nucleic acid molecule of (iii);
- (b) a processing module which is covalently linked to the effector module and which comprises a recognition sequence for a protease; and
- (c) a targeting module which is covalently linked to the processing module and which specifically binds to the surface of a cell, thereby mediating internalization of the fusion protein into the cell.

35. (Amended) The nucleic acid molecule of claim 34, wherein the processing module comprises one of a mistletoe lectin propeptide having SEQ ID NO: 6, a fragment thereof, and a derivative thereof.

36. (Amended) A nucleic acid molecule encoding a fusion protein which comprises

- (a) an effector module which is intracellularly cytotoxic;
- (b) a processing module which is covalently linked to the effector module and which comprises a recognition sequence for a protease, wherein the processing module comprises one of a mistletoe lectin propeptide, a fragment thereof, and a derivative thereof, and wherein the mistletoe lectin propeptide is encoded by a nucleic acid molecule selected from the group consisting of:

- (i) a nucleic acid molecule which has a nucleotide sequence encoding at least a fragment of a protein having the amino acid sequence SEQ ID NO: 6;
- (ii) a nucleic acid molecule which has the nucleotide sequence of at least a fragment of SEQ ID NO: 5;

- (iii) a nucleic acid molecule which hybridizes with the nucleic acid molecule of (i) or (ii); and
- (iv) a nucleic acid molecule which is degenerate with respect to the nucleic acid molecules mentioned in (iii); and
- (c) a targeting module which is covalently linked to the processing module and which specifically binds to the surface of a cell, thereby mediating internalization of the fusion protein into the cell.

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Cancel 37. (Amended) The nucleic acid molecule of claim 36, wherein the effector module comprises one of a mistletoe lectin A chain having SEQ ID NO: 2, a fragment thereof, and a derivative thereof.

Please add new claims 47-49, as follows:

47. (New) The nucleic acid molecule of claim 16, wherein the mistletoe lectin B chain has at least one amino acid exchange at an amino acid position selected from the group consisting of positions 68, 70, and 75.

C6. 48. (New) The nucleic acid molecule of claim 37, wherein the exchange is selected from the group consisting of substitution of S at position Y68, substitution of S at position Y70, substitution of S at position Y75, and substitution of S at position F79.

49. (New) A medicament comprising the nucleic acid molecule of claim 1.

In the Abstract of the Disclosure:

At page 84, please delete the section entitled "ABSTRACT OF THE DISCLOSURE" and substitute the following paragraph:

C7 --The invention relates to nucleic acid molecules which encode fusion proteins which contain as components at least one effector module, a processing module and a targeting module. The nucleic acid molecules according to the invention preferably also encode a modulator module and/or an affinity module. The invention furthermore relates to vectors containing these nucleic acid molecules, hosts transformed with the vectors according to the invention, fusion proteins encoded by nucleic acids according to the invention or produced by the hosts according to the invention as well as to medicaments containing the polypeptides or vectors